

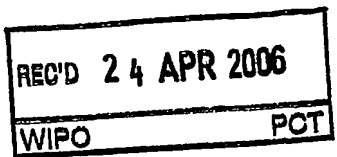
PATENT COOPERATION TREATY


PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)



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|---|--|---|-----------------------|
| Applicant's or agent's file reference 4591PTWO/AG/1a | FOR FURTHER ACTION | | See Form PCT/IPEA/416 |
| International application No. PCT/EP2004/052900 | International filing date (day/month/year) 10.11.2004 | Priority date (day/month/year) 10.11.2003 | |
| International Patent Classification (IPC) or national classification and IPC INV. C07H1/00 C07H5/02 | | | |
| Applicant INALCO S.P.A. et al | | | |
| <p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 5 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> sent to the applicant and to the International Bureau a total of sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p> | | | |
| <p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the report</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input type="checkbox"/> Box No. VIII Certain observations on the international application</p> | | | |
| Date of submission of the demand 12.09.2005 | | Date of completion of this report 25.04.2006 | |
| Name and mailing address of the international preliminary examining authority:  European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016 | | Authorized officer de Nooy, A Telephone No. +31 70 340-2338 | |



**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/EP2004/052900

Box No. I Basis of the report

1. With regard to the **language**, this report is based on
- ☒ the international application in the language in which it was filed
 - ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of:
 - ☐ international search (under Rules 12.3(a) and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4(a))
 - ☐ international preliminary examination (under Rules 55.2(a) and/or 55.3(a))
2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report):*

Description, Pages

1-10 as originally filed

Claims, Numbers

1-23 as originally filed

- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing
3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages
 - ☐ the claims, Nos.
 - ☐ the drawings, sheets/figs
 - ☐ the sequence listing (*specify*):
 - ☐ any table(s) related to sequence listing (*specify*):

* If item 4 applies, some or all of these sheets may be marked "superseded."

**INTERNATIONAL PRELIMINARY REPORT
ON PATENTABILITY**

International application No.
PCT/EP2004/052900

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

| | | |
|-------------------------------|-------------|------|
| Novelty (N) | Yes: Claims | 1-23 |
| | No: Claims | |
| Inventive step (IS) | Yes: Claims | 1-23 |
| | No: Claims | |
| Industrial applicability (IA) | Yes: Claims | 1-23 |
| | No: Claims | |

2. Citations and explanations (Rule 70.7):

see separate sheet

Re Item V

**Reasoned statement with regard to novelty, inventive step or industrial applicability;
citations and explanations supporting such statement**

Reference is made to the following document:

D1: W. Zhang et al. Nucleosides and Nucleotides 18 (1999) 2357-2365

Novelty

The document D1 discloses a synthesis of 1-chloro-3,5-di-toluoyl-deoxy-L-ribofuranoside. The present claims 1, 16-23 differ from this known subject matter in that another route is followed towards the same target compound. The present claims 2-15 differ from this known subject matter in that the same route is followed but the reaction conditions are changed (that is, for the acylation instead of pyridine as in D1, a tertiary amine base in an aprotic solvent is claimed). Thus, claims 1-23 are new in the sense of Article 33(2) PCT.

Inventive step

The present application meets the criteria of Article 33(1) PCT, because the subject-matter of broadest claims 2-15 involves an inventive step in the sense of Article 33(3) PCT.

The document D1 is regarded as being the closest prior art to the subject-matter of claims 2-15, and discloses a synthesis of 1-chloro-3,5-di-toluoyl-deoxy-L-ribofuranoside in which an acylation step is performed with the acylchloride in pyridine.

The subject-matter of claims 2-15 therefore differs from this known subject matter in that an acylation step is performed with an acylchloride in the presence of a tertiary amine in an aprotic solvent AND in that chlorination is done after the esterification step without intermediate work-up (i.e. step v) is performed directly after step iv)).

The technical effect of this difference is the fact that the use of the noxious solvent pyridine is avoided and that a work-up step is avoided.

The problem to be solved by the present invention may therefore be regarded as the provision of an improved method for the synthesis of 1-chloro-3,5-di-toluoyl-deoxy-L-ribofuranoside.

The solution proposed in claims 2-15 of the present application is considered as involving an inventive step (Article 33(3) PCT) for the following reasons:

**INTERNATIONAL PRELIMINARY
REPORT ON PATENTABILITY
(SEPARATE SHEET)**

International application No.

PCT/EP2004/052900

although it is well known to the skilled person that an acylation of an alcohol in a sugar with an acylchloride can be performed in an aprotic solvent in the presence of a tertiary amine instead of pyridine, the additional advantage of being able to perform the chlorination afterwards without intermediate work-up is not obvious nor hinted at in D1.